

It was further demonstrated that peptide analogs to the above neuropeptides could actively and selectively induce cell death in the cancer cells. A formulation of peptide combination termed MuJ-7 has also been described which causes tumor regression in xenotransplanted nude mice. The individual constituent peptides of MuJ-7 were demonstrated to have anticancer activity.

Please replace paragraph 4 on page 2 with the following:

The VIP receptor binding inhibitor VIP₂ (Leu-Met-Tyr-Pro-Thr-Tyr-Leu-Lys) (SEQ ID NO:1) has been shown in our previous studies incorporated in U.S. Patent 6,156,725 to be a selective cytotoxic peptide for cancer cells having receptors for vasoactive intestinal peptide. Novel peptides that have conformational constraints and resist enzymatic degradation are formed by replacing any of the amino acids of the sequence Leu-Met-Tyr-Pro-Thr-Tyr-Leu-Lys with D_{xg}. D_{xg} represents cyclic and acyclic dialkylate glycines where the cyclic ring is C₃-C₈ ring and the number of carbon atoms in the alkyl group is from 1 to 6 (methyl to hexyl). Examples are Aib, MeLeu, Di-ethyglycine and its higher homologs, and 1-amino cycloalkane carboxylic acids. Aib represents α-amino-isobutyric acid. Deg represents di-ethyglycine.

Please replace paragraph 1 on page 3 with the following:

Novel peptides include:

- DT-11 Aib-Met-Tyr-Pro-Thr-Tyr-Aib-Lys-OH (SEQ ID NO:2)
- DT-12 D-Leu-Met-Tyr-Pro-Thr-Tyr-Aib-Lys-OH (SEQ ID NO:3)
- DT-13 Leu-Met-Tyr-Pro-Thr-D-Tyr-Leu-Lys-OH (SEQ ID NO:4)
- DT-14 Leu-Met-Tyr-Pro-Thr-Tyr-D-Leu-Lys-OH (SEQ ID NO:5)
- DT-15 Leu-Met-D-Tyr-Pro-Thr-Tyr-D-Leu-Lys-OH (SEQ ID NO:6)
- DT-16 D-Leu-Met-Tyr-Pro-Thr-Tyr-D-Leu-Lys-OH (SEQ ID NO:7)
- DT-18 Aib-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO:8)
- DT-19 D-Leu-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO:9)

where Deg and Aib are as defined above.

Please replace paragraph 2 on page 3 with the following:

E4
The bombesin antagonist BOM₁ (D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-NH₂) (SEQ ID NO:10) has been shown in our previous studies incorporated in U.S. Patent 6,156,725 to be a selective cytotoxic peptide for cancer cells having receptors for bombesin. Novel peptides that have conformational constraints and resist enzymatic degradation are formed by replacing any of the amino acids of the sequence D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-NH₂ (SEQ ID NO:10) with D_xg where D_xg is defined above. Leucine may be replaced with isoleucine and tryptophan may be replaced by D-Tryptophan.

Please replace paragraph 1 on page 4 with the following:

E6
The Substance P analog (D-Arg-Pro-Lys-Pro-D-Phe-Gln-D-Trp-Phe-D-Trp-Leu-Leu-NH₂) (SEQ ID NO:18)) has been shown in our previous studies incorporated in U.S. Patent 6,156,725 to be a selective cytotoxic peptide for cancer cells having receptors for Substance P. Novel peptides that have conformational constraints and resist enzymatic degradation are formed by replacing any of the amino acids of the sequence D-Arg-Pro-Lys-Pro-D-Phe-Gln-D-Trp-Phe-D-Trp-Leu-Leu-NH₂ (SEQ ID NO:18) with D_xg or Aib. D_xg and Aib are as defined above. Analogs may be 5 to 11 amino acids.

Please replace paragraph 2 on page 4 with the following:

Novel peptides include:

- E6
- DT-31 Aib-Met-Gln-Trp-Phe-Aib-NH₂ (SEQ ID NO:19)
 - DT-32 Deg-Met-Gln-Trp-Phe-Aib-NH₂ (SEQ ID NO:20)
 - DT-33 D-Leu-Met-Gln-Trp-Phe-Aib-NH₂ (SEQ ID NO:21)
 - DT-34 D-Arg-Pro-Lys-Pro-Aib-Gln-D-Trp-Phe-D-Trp-Aib-Leu-NH₂
(SEQ ID NO:22)
 - DT-35 Arg-Pro-Aib-Pro-D-Phe-Gln-D-Trp-Phe-D-Trp-Leu-Leu-NH₂
(SEQ ID NO:23)

where Deg and Aib are as defined above.

Please replace paragraph 3 on page 4 with the following:

E¹

The somatostatin analog (Ala-Gly-Cys-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys (disulfide bridges: 3-14) (SEQ ID NO:24) has been shown in our previous studies incorporated in U.S. Patent 6,156,725 to be a selective cytotoxic peptide for cancer cells having receptors for Somatostatin. Novel peptides that have conformational constraints and resist enzymatic degradation are formed by replacing any of the amino acids of the sequence (Ala-Gly-Cys-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys (disulfide bridges:3-14) (SEQ ID NO:24) with Dxx or Aib where Dxx and Aib are as described above.

Please replace paragraph 2 on page 5 with the following:

E⁸

The somatostatin analog (D-Phe-Cys-Tyr-D-Trp-Orn-Thr-Pen-Thr-NH₂) (SEQ ID NO:26) has been shown in our previous studies incorporated in U.S. Patent 6,156,725 to be a selective cytotoxic peptide for cancer cells having receptors for Somatostatin. Novel peptides that have conformational constraints and resist enzymatic degradation are formed by replacing any of the amino acids of the sequence D-Phe-Cys-Tyr-D-Trp-Orn-Thr-Pen-Thr-NH₂ (SEQ ID NO:26) with Dxx or Aib where Dxx and Aib are as defined above.

In the Claims

Please amend the following claims:

E⁹

Claim 1 (Twice Amended) A peptide of the sequence Leu¹-Met²-Tyr³-Pro⁴-Thr⁵-Tyr⁶-Leu⁷-Lys⁸ (SEQ ID NO:1) wherein at least one of the amino acids at positions 1-8 is replaced by Deg.

Claim 2 (Once Amended) A peptide having the sequence selected from the group consisting of:

Aib-Met-Tyr-Pro-Thr-Tyr-Aib-Lys-OH (SEQ ID NO: 2);
D-Leu-Met-Tyr-Pro-Thr-Tyr-Aib-Lys-OH (SEQ ID NO:3);
Leu-Met-Tyr-Pro-Thr-D-Tyr-Leu-Lys-OH (SEQ ID NO: 4);

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Leu-Met-Tyr-Pro-Thr-Tyr-D-Leu-Lys-OH (SEQ ID NO: 5);
Leu-Met-D-Tyr-Pro-Thr-Tyr-D-Leu-Lys-OH (SEQ ID NO: 6);
D-Leu-Met-Tyr-Pro-Thr-Tyr-D-Leu-Lys-OH (SEQ ID NO: 7);
Aib-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO: 8); and
D-Leu-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO: 9).

210
Claim 33 (Amended) A method for treating breast cancer comprising administering an effective amount of a peptide selected from the group consisting of:

Aib-Met-Tyr-Pro-Thr-Tyr-Aib-Lys-OH (SEQ ID NO:2);
D-Leu-Met-Tyr-Pro-Thr-Tyr-Aib-Lys-OH (SEQ ID NO:3);
Leu-Met-Tyr-Pro-Thr-D-Tyr-Leu-Lys-OH (SEQ ID NO:4);
Leu-Met-Tyr-Pro-Thr-Tyr-D-Leu-Lys-OH (SEQ ID NO:5);
Leu-Met-D-Tyr-Pro-Thy-Tyr-D-Leu-Lys-OH (SEQ ID NO:6);
Aib-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO:8); and
D-Leu-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO:9).

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Claim 35 (Amended) A method for treating colon cancer comprising administering a peptide selected from the group consisting of:

Leu-Met-D-Tyr-Pro-Thr-Tyr-D-Leu-Lys-OH (SEQ ID NO: 6);
D-Leu-Met-Tyr-Pro-Thr-Tyr-D-Leu-Lys-OH (SEQ ID NO: 7);
Aib-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO: 8); and
D-Leu-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO: 9).

212
Claim 34 (Amended) A method for treating breast cancer comprising administering an effective amount of a peptide selected from the group consisting of:

Leu-Met-D-Tyr-Pro-Thy-Tyr-D-Leu-Lys-OH (SEQ ID NO:6);
D-Leu-Met-Tyr-Pro-Thr-Tyr-D-Leu-Lys-OH (SEQ ID NO:7);
Aib-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO:8); and
D-Leu-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO:9).

Claim 36 (Amended) A method for treating prostate cancer comprising administering a peptide selected from the group consisting of:

D-Leu-Met-Tyr-Pro-Thr-Tyr-Aib-Lys-OH (SEQ ID NO:3);
Aib-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO:8); and
D-Leu-Met-Tyr-Pro-Thr-Tyr-Deg-Lys-OH (SEQ ID NO:9).